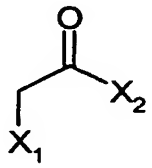
Claims:

1. Process for the preparation of a N-(N'-substituted glycyl)-2-cyanopyrrolidine comprising at least

(a) reacting, in the presence of dimethylformamide, a compound of formula (V)



(V)

wherein, independently of each other, X_1 and X_3 are halogen; X_2 is halogen, OH, O-C(=O)-CH_2X_3, -O-SO_2-(C_{1-8})alkyl or -O-SO_2-(aryl),

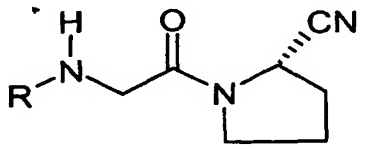
with L-prolinamide, followed by

(b) reacting the resultant compound without isolation with a dehydration agent, optionally followed by

(c) reacting, in the presence of a base, the resultant compound without isolation with an appropriate amine and

(d) recovering the resultant compound in free form or in acid addition salt form.

2. A process according to claim 1 wherein the N-(N'-substituted glycyl)-2-cyanopyrrolidine is a compound of formula (I)



(I)

wherein R is

a) $R_1R_{1a}N(CH_2)_m$ - wherein

R_1 is a pyridinyl or pyrimidinyl moiety optionally mono- or independently disubstituted with (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen, trifluoromethyl, cyano or nitro; or phenyl optionally mono- or independently disubstituted with (C_{1-4})alkyl, (C_{1-4})alkoxy or halogen;

R_{1a} is hydrogen or (C_{1-8})alkyl; and

m is 2 or 3;

b) (C_{3-12})cycloalkyl optionally monosubstituted in the 1-position with (C_{1-3})hydroxyalkyl;

c) $R_2(CH_2)_n$ - wherein either

R_2 is phenyl optionally mono- or independently di- or independently trisubstituted with (C_{1-4})alkyl, (C_{1-4})alkoxy, halogen or phenylthio optionally monosubstituted in the phenyl ring with hydroxymethyl; or is (C_{1-8})alkyl; a [3.1.1]bicyclic carbocyclic moiety optionally mono- or plurisubstituted with (C_{1-8})alkyl; a pyridinyl or naphthyl moiety optionally mono- or independently disubstituted with (C_{1-4})alkyl, (C_{1-4})alkoxy or halogen; cyclohexenyl; or optionally substituted adamantyl; and

n is 1 to 3; or

R_2 is phenoxy optionally mono- or independently disubstituted with (C_{1-4})alkyl, (C_{1-4})alkoxy or halogen; and

n is 2 or 3;

d) $(R_3)_2CH(CH_2)_2$ - wherein each R_3 independently is phenyl optionally mono- or independently disubstituted with (C_{1-4})alkyl, (C_{1-4})alkoxy or halogen;

e) $R_4(CH_2)_p$ - wherein R_4 is 2-oxopyrrolidinyl or (C_{2-4})alkoxy and p is 2 to 4;

f) isopropyl optionally monosubstituted in 1-position with (C_{1-3})hydroxyalkyl; or

g) R_5 wherein R_5 is: indanyl; a pyrrolidinyl or piperidinyl moiety optionally substituted with benzyl; a [2.2.1]- or [3.1.1]bicyclic carbocyclic moiety optionally mono- or multi-substituted with (C_{1-8})alkyl; adamantyl; substituted adamantyl ;or (C_{1-8})alkyl optionally mono- or independently plurisubstituted with hydroxy, hydroxymethyl or phenyl optionally mono-or independently disubstituted with (C_{1-4})alkyl, (C_{1-4})alkoxy or halogen;

in free form or in acid addition salt form.

3. A process according to claim 1 or 2 wherein the dehydration agent of step (b) is a (haloalkylene)dialkylammonium halogenid.

4. A process according to claim 1 or 2 wherein the dehydration agent of step (b) is (chloromethylene)dimethylammonium chloride.

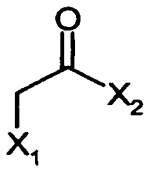
5. A process according to claim 2 wherein the amine of step (c) is a compound of formula (VI)

H_2NR (VI)

wherein R is as defined for formula (I) in claim 2.

6. A process according to claim 2 comprising

(a) reacting, in the presence of dimethylformamide, a compound of formula (V)



(V)

wherein X_1 is halogen; X_2 is halogen, OH, O-C(=O)-CH_2X, -O-SO_2-(C_{1-8})alkyl or -O-SO_2-(aryl), with L-prolinamide, followed by

(b) reacting the resultant compound without isolation with

(chloromethylene)dimethylammonium chloride, followed by

(c) reacting, in the presence of a base, the resultant compound without isolation with a compound of formula (VI)

H_2NR (VI)

wherein R is as defined for formula (I) and

(d) recovering the resultant compound in free form or in acid addition salt form.

7. A process according to claim 6 wherein R is $R_2(CH_2)_n$- and R_2 is substituted adamantyl; and n is 0, 1, 2 or 3.

8. A composition of N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine, obtainable according to the process of claim 1 or 2, whereby 95% to 99,9% is N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and 5% to 0,1% is N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine, especially whereby 98% to 99,99% is N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and 2% to 0,01% is N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine.

9. A composition comprising a N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and a N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine, whereby 98% to 99,9% is N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and 2% to 0,1% is N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine, preferably whereby 98% to 99,99% is N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and 2% to 0,01% is N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine, most preferably whereby 99% to 99,99% is N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and 1% to 0,01% is N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine.

10. A composition of N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine and N-(N'-substituted glycyl)-2(R)-cyanopyrrolidine, obtainable according to the process of claim 1 or 2.

11. A pharmaceutical composition comprising,

a) one or more pharmaceutically acceptable excipients, and

b) at least one N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine obtainable according to the process of claim 1 or 2.

12. A pharmaceutical composition comprising,

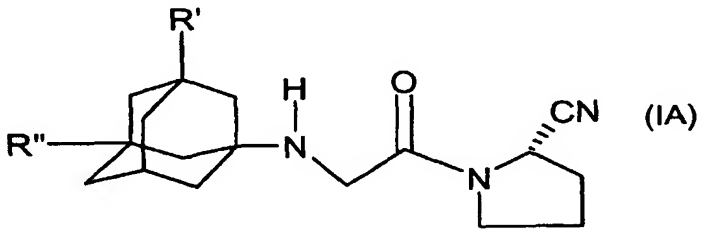
a) one or more pharmaceutically acceptable excipients, and

b) at least one N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine, and

c) between 0.00001% and 5% by weight of at least one (haloalkylene)dialkylammonium halogenid.

13. A composition according to claim 12, wherein the N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine is obtainable according to the process of claim 1 or 2.

14. A composition according to any of claim 8 to 13, whereby the N-(N'-substituted glycyl)-2(S)-cyanopyrrolidine is a compound of the formula



(IA)

wherein R' is hydroxy and R'' is hydrogen in free form or in acid addition salt form.